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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,069	03/14/2007	Stephen John Kent	00704-8010.US00	6553

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EXAMINER
JUEDES, AMY E

ART UNIT	PAPER NUMBER
1644	

NOTIFICATION DATE	DELIVERY MODE
11/16/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentprocurement@perkinscoie.com

Office Action Summary	Application No.	Applicant(s)	
	10/560,069	KENT, STEPHEN JOHN	
	Examiner	Art Unit	
	AMY E. JUEDES	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 September 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *53-67 and 69-88* is/are pending in the application.

4a) Of the above claim(s) *69-72,84 and 85* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *53-67,73-83 and 86-88* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/13/10, 3/8/10, 12/10/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment and remarks, filed 9/13/10 and 12/10/09, are acknowledged.

Claims 53, 56, 69-70, 72, and 86-88 have been amended.

Claim 68 has been cancelled.

Claims 80-88 have been added.

Claims 53-67 and 69-88 are pending.

2. Applicant's election with traverse of HIV as the species of antigen, in the reply filed on 9/13/10, is acknowledged.

Applicant's traversal is on the grounds that unity of invention exists, since the Pryjma reference fails to teach a *pharmaceutical composition* for modulating an immune response, as recited in the amended claims, since the composition of Pryjma et al. comprise FCS. Applicant notes that the skilled artisan would understand that FCS proteins can cause an adverse immune response and should be avoided in cell therapy applications. Thus, Applicant concludes that the monocyte compositions of Pryjma et al. do not meet the limitation of a pharmaceutical composition. The instant specification on page 38 discloses that pharmaceutically acceptable carriers may be the growth medium in which cells are grown. Thus, the pharmaceutical carrier of the instant claims would appear to encompass cell culture medium, as taught by Pryjma et al. Nevertheless, the instant claims, as amended, lack unity of invention over the prior art references cited below.

The requirement is still deemed proper and is therefore made FINAL.

Claims 69-72 stand withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Claims 84-85 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected species.

Claims 53-67, 73-83 and 86-88 are being acted upon.

3. The rejection of the claims under 35 U.S.C. 103 is withdrawn in view of Applicant's amendment to the claims. Specifically, Jager et al. do not teach 12-20 amino acid peptides or overlapping peptides of a target antigen of a pathogenic organism, as recited in the amended claims.

4. Claim 67 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 67 depends from claims 53 and 61, which require contacting the antigen presenting cells with an antigen corresponding to a target antigen of a pathogenic organism. However, claim 67 recites that the cells are contacted with an alloantigen, cancer antigen, an autoantigen, or an allergen. Thus, the antigens recited in claim 67 are broader than those required by independent claim 53. For example, an autoantigen is not an antigen of a pathogenic organism.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 53-67 and 73-79 stand rejected and claims 80-83, and 86-88 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

a composition for modulating an immune response in a subject to a target antigen, said composition comprising antigen-presenting cells, including whole blood, fresh blood, or fractions thereof including peripheral blood mononuclear cells, buffy coat fractions of whole blood, irradiated blood, dendritic cells, monocytes, macrophages, lymphocytes, and neutrophils,

does not reasonably provide enablement for:

a composition for modulating an immune response in a subject to a target antigen, said composition comprising precursors of antigen-presenting cells, or comprising packed red cells.

As set forth previously, The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention, *in re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

"The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling (MPEP 2164.03)" The MPEP further states that physiological activity can be considered inherently unpredictable.

The instant claims are drawn to a composition for modulating an immune response in a subject to a target antigen, wherein the composition comprises an antigen presenting cells presenting the antigen. Antigen presenting cells including dendritic cells, monocytes/macrophages, and B cells express MHC class II molecules and are known to process and present antigen to T cells (see Vidard et al., 1992). Said APCs are readily available in the blood. Thus blood populations such as PBMC, whole blood, etc. would comprise significant numbers of APCs and could conceivably be used as a source of APC for inducing an immune response. However, the instant claims encompass compositions comprising non-conventional antigen presenting cells such as red cells,. While it is conventional in the art to use antigen presenting cells to induce an antigen specific immune response, red cells are not known as antigen presenting cells. For example, red cells do not even express MHC molecules, and would be unlikely to function to modulate and in vivo immune response to an antigen. Furthermore, the claims encompass compositions for modulating an in vivo antigen specific immune response comprising antigen presenting cell precursors. For example, antigen presenting cells such as B cells, develop from, hematopoietic stem cell precursors through a variety of stages (See Janeway and Travers). However, the use of B cell precursors as antigen presenting cells would be highly unpredictable. In fact, B cell precursors can even be susceptible to apoptosis after antigen encounter (see Janeway and Travers, page 5:4).

Thus, given the unpredictability of the art, the instant specification must provide a sufficient and enabling disclosure commensurate in scope with the instant claims. The specification provides examples that antigen pulsed PBMC can be used to modulate and antigen specific immune response in vivo. PBMC comprise many types of antigen presenting cells including dendritic cells, B cells, and macrophages. However, the specification does not

provide any evidence that other types of non-conventional APCs such red cells, or antigen presenting cell precursors can function to modulate an antigen specific immune response in vivo. Thus, given the unpredictability of the art, the breadth of the instant claims, and the lack of guidance provided by the instant specification, it would require undue experimentation to make and use the compositions as claimed.

Applicant's arguments field 12/10/09 have been fully considered, but they are not persuasive.

Applicant argues that as evidenced by Mascaretti et al., packed red cell preparations containing various lymphocyte subsets, and would be expected to function the same as PBMC populations in presenting antigen.

Mascaretti et al. teach that white blood cell content in packed red cell preparations is variable and depends of the method of isolation used. In some isolation method, white blood cells are very infrequent. Furthermore, Mascaretti et al. only characterize the presence of T cells, and no evidence has been provided that packed red cell preparations comprise cells capable of acting as antigen presenting cells. Furthermore, there is no evidence that a cell population comprising packed red cells and a minority of white blood cells can function as a composition for modulating an immune response in a subject, as claimed. Moreover, the instant claims specifically recite that the antigen presenting cells are the packed red cell fraction of whole blood. This encompasses a pure red cell fraction (i.e. devoid of white blood cells). There is no evidence that packed red cell populations can function as a composition for modulating an immune response in a subject, and based on the unpredictability of the art, it would require undue experimentation to use the compositions as broadly claimed.

Applicant further argues that antigen presenting cell precursors which can capture endogenous antigens and present the antigen to T cells were well known in the art, as evidenced by Steinman et al. and Mitchell et al.

It is conceded that antigen presenting cell precursors that can be differentiated into antigen presenting cells were known in the art. For example, CD34+ stem cells are a precursor cell that can differentiate in vitro to antigen presenting dendritic cells. However, the instant claims are drawn to a composition for modulating an immune response in a subject comprising said precursors. As noted in the original rejection, the ability of such a precursor cell to function to modulate an immune response in a subject

is highly unpredictable. Applicant has not provided any evidence that such a composition can function as claimed. For example, Mitchell et al. demonstrate that immature dendritic cell precursors can present antigen after 24 hour culture in GM-CSF to mature and activate the cells to differentiate into dendritic cells. However, the instant claims are drawn to a non-activated antigen presenting cell precursor population that can modulate an immune response in a subject. Applicant has not provided any evidence that a non-activated antigen presenting cell precursor population, including non-differentiated hematopoietic stem cells, can function to modulate an immune response in a subject, as claimed.

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 53-62, 64-67, and 73-78 stand rejected, and claims 80-83 and 88 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent 6,080,399.

As set forth previously, The '399 patent teaches a composition for inducing an antigen specific immune response in a subject comprising antigen presenting cells, including PBMC, that have been pulsed with peptides (i.e. proteinaceous molecules, see column 4, 7 and 29, in particular). The '399 patent teaches that the PBMC can be freshly isolated and pulsed with peptide by incubating the PBMC with peptide for 1 hr in PBS (see column 41 in particular). Thus, the peptide pulsed PBMC have not been activated, since they have been incubated in PBS in the absence of cytokines or other activation stimuli. Additionally, the PBMC, after only a 1 hour incubation, would inherently have increased less than about 5% in cell number, since they have been processed under identical conditions to those recited in the instant claims. The '399 patent teaches peptides derived from tumor proteins (i.e. proteins expressed by cancer cells, see column 4-5, in particular). The '399 patent teaches that the APCs can be loaded with more than one peptide fragment of an antigen (i.e. a "set" of peptides, see columns 4-5 in particular). The '399 patent also teaches that the peptides can comprise more than one fragment of more than 1 type of protein antigen (i.e. a least 2 "sets" of peptides derived from a distinct polypeptide or non-overlapping peptides, see column 4-5 in particular). The '399 patent also teaches using peptides that bind to class I MHC or class II MHC molecules (i.e. peptides selected to enhance a cytolytic T lymphocyte or T helper lymphocyte response). The '399 patent also teaches using a plurality of distinct peptides with different amino acid substitutions (i.e. peptides displaying partial sequence identity or overlapping peptides that comprise "different" portions of an amino acid sequence of a single

polypeptide, see column 22 in particular). Additionally, the '399 patent teaches that only certain, but not most, amino acids should be substituted (i.e. less than 50%). Thus, the substituted peptides have been "derived from" at least 30% of the starting peptide (i.e. a polypeptide of interest).

Applicant's arguments filed 12/10/09 have been fully considered, but they are not persuasive.

Applicant argues that the compositions of the '399 patent comprise IL-12, whereas the compositions of the instant claims are capable of modulating the immune response in the absence of IL-12.

The instant claims are drawn to a pharmaceutical composition "comprising" an antigen presenting cell. The term "comprising" is open ended and does not exclude unrecited elements, such as IL-12. Thus, the instant claims encompass compositions of antigen presenting cells and IL-12 as taught by the '399 patent, and are not limited to compositions consisting of antigen presenting cells excluding IL-12, as asserted by Applicant.

Applicant further argues that the '399 patent does not teach a target antigen of a pathogenic organism.

The '399 patent teaches that the APCs are pulsed with peptide antigens derived from infectious agents such as viruses, including HIV (see column 5, in particular). Additionally, claim 88 is included since the '399 patent teaches freshly isolated peripheral blood cells (i.e. a composition comprising "fresh blood" cells).

8. The following are new grounds of rejection necessitated by Applicant's amendment.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 87 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 87 recites the limitation "the target antigen" in line 7. There is insufficient antecedent basis for this limitation in the claim.

10. Claims 86-87 are rejected under 35 U.S.C. 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically:

A composition comprising antigen presenting cells, wherein the composition “excludes IL-12”

Applicant indicates that support for a composition excluding IL-12 can be found in New Generation Vaccines, which is incorporated by reference.

A review of the specification fails to reveal support for the new limitations.

Any negative limitation must have basis in the original disclosure. The mere absence of a positive recitation is not basis for exclusion (see MPEP 2173.05(i). While positively recited alternative elements may be explicitly excluded in the claims, the instant specification does not disclose the claimed compositions optionally comprising IL-12. While Applicant notes that the material is disclosed in New Generation Vaccines, incorporated by reference, essential material that is necessary to provide a written description of the claimed invention may only be by way of an incorporation by reference to a U.S. Patent of patent application. Thus, the specification does not adequately describe a composition that "excludes IL-12”, as now claimed.

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 53-61, 63, 65-67, 73-75, 76-83, and 86-88 are rejected under 35 U.S.C. 102(b) as being anticipated by Venturini et al., 2002.

Venturini et al. teach a composition comprising PBMC as antigen presenting cells for modulating a T cell response, wherein said PBMC have been incubated with HIV peptides for 2 hours (see page 6988, in particular). Venturini et al. teach the PBMCs in R10-HS culture medium (see page 6988, paragraph 5, right column). Said R10-HS culture medium comprises RPMI medium supplemented with human serum (see page 6988). The instant specification on page 38 teaches that pharmaceutically acceptable carriers are those which are non-toxic including growth medium which cells are grown. Thus, the R10-HS culture medium of Venturini et al. meets the limitation of a pharmaceutically acceptable carrier. Venturini et al. teach contacting the PBMC with a mixture of peptides (i.e. a peptide set) comprising overlapping 20-mer peptides of HIV-1 Gag (see page 6988, in particular). Venturini et al. teach that the peptide mixture comprises peptides covering the whole sequence of the Gag protein i.e. derived from at least 30% of the polypeptide of interest, see page 6989, in particular). The peptides of Venturini et al. overlap at either ends of the peptides (see Table 1, in particular). Venturini et al. teach irradiated PBMC (i.e. antigen presenting cells comprising irradiated blood cells). Furthermore, the peptide pulsed PBMC of Venturini et al. have not been activated, since they have been incubated in the absence of cytokines or other activation stimuli. Additionally, the PBMC, after only a 2 hour incubation, would inherently have increased less than about 5% in cell number, since they have been processed under identical conditions to those recited in the instant claims. Furthermore, even though Venturini et al. do not teach incubating the cells for less than an hour with peptide, the instant claims are drawn to a product, a composition comprising non-activated antigen presenting cells presenting a peptide. The patentability of a product does not depend on its method of production in the absence of a structural difference. In the instant claims, the composition of Venturini et al. is identical to that of the instant

claims. Furthermore, the intended use limitations of the instant claims, wherein the composition is to be used for inducing an immune response in a subject, or as a vaccine do not carry patentably weight in the absence of a structural difference. The composition of Venturini et al. is structurally identical to that of the instant claims.

Thus, the reference clearly anticipates the invention.

12. No claim is allowed.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy E. Juedes, whose telephone number is 571-272-4471. The examiner can normally be reached on 8am to 4:30pm, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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